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10/683,990	10/10/2003	James McSwiggen	MBHB04-736 (400/134)	3438

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/683,990	**Applicant(s)** MCSWIGGEN ET AL.	
	Examiner Janet L. Epps-Ford	**Art Unit** 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,13-21,30 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,13-21,30 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. In the restriction requirement mailed 6-14-06 it was stated: "[A]pplicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention. The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse."

2. In the response filed 9-14-06 Applicants did not make an election, Applicants merely cancelled claim 2 (directed to group I), and have amended claims 1, 3, 13-21, 30 and 33 to recite an "siRNA molecule". Although Applicants did not actually make an election, Applicant's amendment of 9-14-06 is effectively treated as an election of group II (as defined in the restriction requirement), with traverse. Applicant traversed the restriction on the grounds that the specification demonstrates that double stranded nucleic acid molecules that lack ribonucleotides are capable of mediating RNA interference similar to double stranded nucleotides that have ribonucleotides. Applicant's argument of common function shared among groups I and II is not found persuasive, for the reasons of record, and since the two inventions do not share a common chemical structure, such that the search thereof would have been coextensive in scope.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1 3, 13-21, 30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carmeliet et al. (WO 01/85796 A2), in view of GenBank Accession No. NM_002632, Hammond et al. (2001), Elbashir et al. (EMBO Journal 2001, vol. 20, pages 6877-6888) and Parrish et al. (Molecular Cell 2000, vol. 6, pages 1077-1087).

The teachings of Carmeliet et al. aims to provide research tools for the study of pathological angiogenesis. In one particular embodiment, this invention aims at providing antagonist of placental growth factor (PGF): see page 8, lines 1-14 of this reference:

Also within the scope of the invention are oligoribonucleotide sequences, that include anti-sense RNA and DNA molecules and ribozymes that function to inhibit the translation of VEGFR-1 mRNA or PIGF mRNA. Anti-sense RNA and DNA molecules act to directly block the translation of mRNA by binding to targeted mRNA and preventing protein translation. In regard to antisense DNA, oligodeoxyribonucleotides derived from the translation initiation site, e.g., between -10 and +10 regions of the VEGFR-1 or PIGF nucleotide sequence, are preferred. Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. The mechanism of ribozyme action involves sequence specific hybridization of the ribozyme molecule to complementary target RNA, followed by a endonucleolytic cleavage. Within the scope of the invention are engineered hammerhead motif ribozyme molecules that specifically and efficiently catalyze endonucleolytic cleavage of VEGFR-1 or PIGF RNA sequences.

However, this reference does not disclose the specific nucleotide sequence encoding human placental growth factor 1 of SEQ ID NO: 257, as recited in the instant claims.

The sequence of human placental growth factor 1 set forth in SEQ ID NO: 257 was previously disclosed in GenBank Accession No. NM_002632.

Hammond et al. teach that antisense and RNA interference are two methods of silencing expression of a gene and that RNA interference possesses characteristics that make it superior to antisense. On page 110, first column, Hammond teaches that antisense methods are straightforward but suffer from "questionable specificity and incomplete efficacy". RNA interference on the other hand, "has been shown in diverse organisms to inhibit gene expression in a sequence-specific manner" (same page and column) and requires only a few molecules of dsRNA per cell to silence expression.

Hammond also teaches that the RNA interference phenomenon in animals was discovered by researchers who were using antisense techniques and found that the use of double stranded instead of single-stranded RNAs reduced gene expression tenfold more efficiently (see paragraph bridging pages 110-111). Hammond et al. do not teach use of siRNAs.

Elbashir et al. teach that RNA interference is mediated efficiently by chemically synthesized RNAs that are 21-23 nucleotides in length and name these short duplexes “short interfering RNAs” (siRNAs). These siRNAs are formulated into compositions with a pharmaceutically acceptable carrier for transfection into cells. Elbashir et al. also teach that siRNAs containing nucleotide modifications known in the art such as 2’-OMe substitutions can stimulate RNA interference. Parrish et al. teach that some common nucleotide modifications, including sugar modifications such as 2’-fluoro, base modifications such as 5-modified uridines and phosphorothioate backbones are tolerated in interfering RNAs.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the cited references to make double stranded RNAs that are optionally modified siRNAs capable of down-regulating the placental growth factor-1 gene (PGF-1). Carmeliet et al. teach the use of nucleic acid based inhibitors, including antisense DNA and RNA as a means to antagonize the activity of PGF-1. Hammond et al. teach that the use of dsRNA as a means to inhibit the expression is superior to the use of antisense. Elbashir et al. provide a motivation to make a double stranded RNA as an siRNA, teaching that siRNAs are efficient mediators of RNA interference. Parrish et al. provide a motivation to use siRNAs containing modified sugar, base and backbone modifications, teaching that such modifications, which are well-known and routinely used in the antisense field, are tolerated in RNA interference. One of ordinary skill in the art would have had a reasonable expectation of success in making siRNA to down-regulate the expression of the PGF-1 gene because Carmeliet et al. teach that PGF-1 gene expression can be inhibited by the activity of RNA inhibitors, and Hammond et all., Elbashir et al. and Parrish et al. teach the feasibility of designing a dsRNA molecule to inhibit the activity of a target gene having a known nucleotide sequence (see GenBank Accession No. NM_002632). One of ordinary skill in the art would have had a reasonable expectation of success in making siRNAs having sugar, base and backbone modifications because Elbashir et al. and Parrish et al. each teach that interfering RNAs containing such modifications are active in provoking RNA interference.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1 3, 13-21, 30 and 33 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-35 of copending Application No. 10/922,761. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-31 of the copending application are broadly drawn to siRNA targeting placental growth factor comprising various modifications, and further wherein said placental growth factor is defined by NM_002632, and the instant claims are also drawn to siRNA targeting PGF-1 and further wherein said PGF-1 is defined by NM_002632 (see copending claim 32) or SEQ ID NO: 257 (as set forth in the instant application). Absent evidence to the contrary, the claims of the instant application, and those of the copending application both read on common subject matter, however the claims of instant application are limited to wherein PGF-1 is defined by SEQ ID NO: 257, however this sequence is also disclosed in the claims of the copending application, particularly claim 32, therefore the instant claims read on an obvious alternative embodiment of the claims of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Epps-Ford

Janet L. Epps-Ford, Ph.D.
Primary Examiner
Art Unit 1633

JLE